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10/574,054	06/07/2006	Youe-Kong Shue	8031-011-US	7988

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EXAMINER	
KRISHNAN, GANAPATHY	
ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,054	SHUE ET AL.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/14/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A Request for Continued Examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed 9/1/2009 has been entered.

The Request for Continued Examination filed 9/1/2009 has been carefully considered. The following have been made of record in the RCE:

1. Claims 31-33 have been canceled.

2. Claim 1 has been amended.

3. Remarks drawn to rejections under 35 USC 112, second paragraph, 102 and 103.

The following rejections has been withdrawn:

1. The rejection of Claims 1-7 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been overcome by amendment to Claim 1 by deletion of the term 'further'. The recitation of the said term in the claim previously meant that the administration of the aminosugar is an additional step in the claimed method of treatment, which is performed after a treatment step that precedes it, which (the preceding step) was not recited. The amendment as instantly done clarifies the claim.

2. The rejection of Claims 1-30 under 35 U.S.C. 103(a) as being unpatentable Henderson (US 5,587,363) in view of Speck (US 4,870,061), Nanba et al (US 5,169,636), Burger (US

5,843,919), Woerly (US 5,863,551), Evans et al (US 6,506,785) and Wong et al (WO 00/68194) has been withdrawn and the new103 rejection contained herein below is made of record.

Claims 1-30 are pending in the case.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 18-19, 22-24 and 27-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Henderson (US 5,587,363, of record).

Henderson teaches the administration of compositions comprising glucosamine for the treatment of connective tissue and cartilage repair (co. 4, lines 47-63; due to degradation-pathological marker as recited in instant claims 18-19, 22-24) and arthritis/pain. The aminosugar can be glucosamine or N-acetyl glucosamine or galactosamine or their salts (col. 3, line 34 through col. 4, lines 16-63; col. 6, lines 49-56; col. 8, Case #1; col. 6, lines 48-56; col. 7, lines 57-61, limitations of claims 27-28). According to Henderson, connective tissues of humans and animals are constantly subjected to stresses and strains that can result in afflictions such as arthritis, joint inflammation (col. 1, lines 23-31). Repair is done by manufacture of collagen, which needs proteoglycans and for the production of proteoglycans glucosamine is needed (col.

1, line 54 through col. 2, line 51). Glucosamine is also known to localize in cartilage and joint tissues (col. 4, lines 47-52). Henderson also teaches dosages of the aminosugars for the said treatments (col. 8, lines 1-49; col. 11 line 15 through col. 12, line 46). This teaching of Henderson is seen to meet the limitations of the said claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 10-11, 18-22, 24-25 and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weidner (WO 03/002117, newly cited) in view of Speck (US 4,870,061, of record) and Nanba et al (US 5,169,636, of record).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following rejections cover limitations not covered by the anticipation rejection above.

Weidner, drawn to aminosugar comprising compositions, teach the treatment of osteoarthritis and synovitis via administration of the said composition comprising effective amounts of the aminosugar(s) to individuals suffering from osteoarthritis/degenerative arthritis (page 2, lines 15-31; page 20, lines 19-25; limitations of claims 1, 18-22, 24, 25-intramuscular injection; page 19, line 41 through, page 20, line 3). Osteoarthritis is a degenerative joint condition marked by cartilage degradation according to Dictionary.com. Suitable aminosugars for use are glucosamine, galactosamine, their salts and derivatives including N-acetyl derivatives and hydrochloride salts (page 10, lines 30-35, limitations of claims 2, 10, 27. 28-for specific aminosugars). The compositions can be administered as a polymer implant or as an intramuscular injection (page 15, lines 1-10; limitations of claims 3-4, 6, 8 and part of claim 10 and 29). The formulations can be in the form of suspensions and gels (page 15, lines 36-39; limitations of claims 3-5, 7, 8 and part of claim 29). Gel-forming agents and gel bases can also be used (page 17, lines 9-15; this is also seen to teach the limitations of claim 7).

However, Weidner does not specifically teach treatment of osteoarthritis and synovitis via intraarticular administration of their aminosugar compositions as in claims 1 and 10,

compositions in the form of particle, nanosphere, microsphere, pump, controlled release, subcutaneous injection or infusion, the treatment wherein the condition is not osteoarthritis and the combination therapy with antiinflammatory drugs and hexoaminidase inhibitors and the use of iminocyclitols as in claims 2, 4-6, 8-11, 16, 24, 25, 26, 29 and 30 and also the treatment of subchondral bone edema as in claims 1, 12, 14, 19 and 21. But Weidner's teaching indicates that cartilage degradation and synovitis can be treated via administration of aminosugars as instantly claimed via injection even though not specifically via intraarticular injection.

Speck teaches a method of treating degenerative joint disease (joint cartilage degradation) by administration of N-acetyl glucosamine in combination with excipients via intraarticular, intramuscular, intravenous, or other injection or infusion methods (col. 1, lines 1-67; col. 5 line 15 through col. 6, line 34; limitations of claim 10-11 and 25). Speck does not exemplify such a method for treatment of cartilage degradation, synovitis and subchondral bone edema as in instant claims 1, 12-14, 16-17, 19-21, 23-24, via administration of active agents other than N-acetylglucosamine as in instant claims 2 and 27; the various forms of administration as in claims 3-9 and 29 and combination therapy of aminosugars with antiinflammatory drugs and hexoaminidase inhibitors as in claim 30. But the teaching of Speck regarding the mode of administration of N-acetylglucosamine, especially intraarticular and infusion methods for the treatment of cartilage degradation means that the same modes of administration can also be used in the methods of treatment as instantly claimed.

Howe ver, both Weidner and Speck do not teach a method wherein the particle is in the form of a liposome as instant claim 5.

Nanba et al, drawn to liposomes, teach compositions comprising oligosaccharides comprising glucosamine and galactosamine residues entrapped by liposomes (col. 1, lines 60 col. 2, line 68). The liposomes containing the aminosugars are made into particles having a diameter of about 0.03-0.8 microns (microspheres, col. 5, lines 43-46, limitations of claims 4-5 and 8-for matrix). According to Nanba liposomes are models for biological membranes and are effective in stabilizing drugs and achieving sustained release of drugs in vivo. The duration of the efficacy of drugs can be prolonged (col. 1, lines 25-28; lines 37-39). Even though Nanba teaches oligosaccharides comprising glucosamine and galactosamine residues, one of skill in the art will recognize that the monomeric aminosugars can also be used to make the same liposomal formulations as instantly claimed and used in the instant methods of treatment. Nanba teaches only a matrix comprising his aminosugars in the form of liposomal particles and microspheres. Even though he does not teach the use of his compositions for treating synovitis, subchondral bone edema and cartilage degradation one of ordinary skill in the art will recognize that his compositions can be used for that purpose in view of the teachings of Weidner and Speck.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a formulation comprising amino sugars and use it in a method of treatment as instantly claimed since the active agents and the methods of treatment via the different forms and modes of administration using them individually are seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to make compositions comprising aminosugars including various forms of compositions and modes of administration and use them in a method of treatment of cartilage degradation and synovitis and as instantly claimed since active agents like glucosamine, galactosamine are responsible for the synthesis of proteoglycans

needed for cartilage/tissue repair and the said aminosugars are well known agents for the said treatment as taught in the prior art above.

It is well within the purview of one of ordinary skill in the art to adjust ratios and substitute structurally similar active agents and make compositions in different forms since similarity in structure and function/utility entail motivation for use in the instant compositions and methods. One of skill in the art would also be motivated to look for other active agents and formulation that are more efficient and have enhanced beneficial effects.

Claims 4, 7-8 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weidner (WO 03/002117, newly cited) in view of Speck (US 4,870,061, of record) and Burger (US 5,843,919, of record).

The teachings of Weidner and Speck are as above. However, both do not teach a method of treatment that uses the formulation as instantly claimed in the form of an implant, a gel and a combination therapy which includes antiinflammatory drugs.

Burger, drawn to arthritis/osteoarthritis, teaches the treatment of these conditions using compositions comprising a combination of glucosamine and N-acetyl glucosamine (col. 1, lines 14-45; col. 2, lines 19-44). The said compositions are preferably in the form of solutions, suspensions, gels, systemic implant or an injection or injection into an affected joint (col. 3, lines 20-56; limitations of claims 4 and 7-8). According to Burger medications for treatment of osteoarthritis (which involves cartilage degradation) include antiinflammatory compounds (col. 1, lines 32-35, limitation of claim 30). This means that antiinflammatory drugs can be combined with aminosugars for the treatment of cartilage degradation since both are useful for the same

purpose. Even though Burger does not specifically exemplify the said method of treatment wherein the composition is injected intraarticularly his teaching regarding the injection into the affected joint suggests that compositions comprising glucosamine and N-acetylglucosamine including galactosamine and its N-acetyl derivative and antiinflammtory drugs can be directly administered into the affected joints (intraarticular injection).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a formulation comprising amino sugars and use it in a method of treatment as instantly claimed since the active agents and the methods of treatment via the use of forms like gels and implants and modes of administration using them individually are seen to be suggested in the prior art.

One of ordinary skill in the art would be motivated to make compositions comprising aminosugars including various forms of compositions like gels and implants and modes of administration and use them in a method of treatment as instantly claimed since active agents like glucosamine and galactosamine are responsible for the synthesis of proteoglycans needed for cartilage/tissue repair and the said aminosugars are well known agents for such repair and said treatment as taught in the prior art above. Also, gels and implants have the advantage of delivering the active agents directly to site where they are needed.

It is well within the purview of one of ordinary skill in the art to adjust ratios and substitute structurally similar active agents and make compositions in different forms since similarity in structure and function/utility entail motivation for use in the instant compositions and methods. One of skill in the art would also be motivated to look for other active agents and formulation that are more efficient and have enhanced beneficial effects.

Claims 3-4 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weidner (WO 03/002117, newly cited) in view of Speck (US 4,870,061, of record) and Woerly (US 5,863,551, of record).

The teachings of Weidner and Speck are as above. However, both do not teach a method of treatment that uses the formulation as instantly claimed in the form wherein the aminosugar is entrapped in a matrix, a hydrogel and other forms of gels.

Woerly teaches polymer hydrogels as implants for treating tissue replacement and regeneration (col. 1, lines 5-18, limitations of claim 4, 6 and 7-8). Another aspect of his invention is the use of a polymer matrix (col. 5, lines 33-40 and lines 52-56, limitation of 3). The polymer matrices can include aminosugars like glucosamine, N-acetyl glucosamine, galactosamine and N-acetylgalactosamine (col. 8, lines 31-34). Even though Woerly does not exemplify the use of such matrices and gels in a method for the treatment of the conditions as instantly claimed one of skill in the art will recognize that such matrices containing the monomeric aminosugars can be made and used in a method of treatment of degenerative diseases and conditions.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a formulation comprising amino sugars and use it in a method of treatment as instantly claimed since the active agents and the methods of treatment via the use of forms like gels and implants and modes of administration using them individually are seen to be suggested in the prior art.

One of ordinary skill in the art would be motivated to make compositions comprising aminosugars including various forms of compositions like gels and implants and modes of

administration and use them in a method of treatment as instantly claimed since active agents like glucosamine and galactosamine are responsible for the synthesis of proteoglycans needed for cartilage/tissue repair and the said aminosugars are well known agents for such repair and said treatment as taught in the prior art above. Also, gels and implants have the advantage of delivering the active agents directly to site where they are needed.

It is well within the purview of one of ordinary skill in the art to adjust ratios and substitute structurally similar active agents and make compositions in different forms including gels other than hydrogels since similarity in structure and function/utility entail motivation for use in the instant compositions and methods.

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Weidner (WO 03/002117, newly cited) in view of Speck (US 4,870,061, of record) and Wong et al (WO 00/68194 of record).

The teachings of Weidner and Speck are as above. However, both do not teach a method of treatment that uses the formulation that has the aminosugar in combination with hexoaminidase inhibitors.

Wong et al teach that hexoaminidases catalyze a myriad of processes, one of which is cartilage erosion in arthritic subjects from over catabolism of glycosaminoglycans that fill the cartilage tissue. Wong specifically teaches development of iminocyclitols as inhibitors of hexoaminidases (page 1, line 5 through page 2, line 13; page 2, lines 33-39; limitation of claim 30). This means that iminocyclitols can be used in combination with glucosamine and

galactosamine and their salts and their N-acyl derivatives for the treatment of cartilage degradation.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a formulation comprising amino sugars in combination with hexoaminidase inhibitors and use it in a method of treatment as instantly claimed since the individual use of each of the active agents in the methods of treatment as instantly claimed is seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to make compositions comprising aminosugars in combination with hexoaminidase inhibitors and use them in a method of treatment of cartilage degradation and synovitis and as instantly claimed since active agents like glucosamine, galactosamine are responsible for the synthesis of proteoglycans needed for cartilage/tissue repair and iminocyclitols (hexoaminidase inhibitor) is responsible for erosion of cartilage. The use of a combination will have an additive effect in building cartilage since one agent helps build cartilage and the other protects it from erosion.

It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been taught individually in the prior art. See In re Kerkhoven, 205 USPQ 1069, CCPA 1980.

Claims 1, 2,4-5, 7-9, 12, 14, 19, 21 and 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weidner (WO 03/002117, newly cited) in view of Speck (US 4,870,061, of record) and Petrus et al (US 6,656,925, newly cited).

The teachings of Weidner and Speck are as above. However, both do not teach a method of treatment of subchondral bone edema using aminosugars in the form of a controlled release formulation.

Petrus et al, drawn to arthritis, teach that during the inflammatory process vasoactive substances are released at the site of inflammation and cause edema (col. 1, line 36 through col. 2, line 8). Agents for treating cartilage degradation include glucosamine, its salts and N-acetylglucosamine (col. 5, lines 37-60; col. 6, line 14). Suitable routes of administration include subcutaneous, and intramuscular (col. 8, lines 15-17; col. 9, lines 35-36) using compositions in the form of suspensions and gels (col. 8, lines 19-21). In addition to aminosugars antiinflammatory agents can also be used (col. 8, lines 64-65 and col. 9, line 2). Petrus also suggests delivery of the said compositions in the form of controlled release (col. 8, lines 26-30). According to Petrus for patients who have difficulty in oral administration intramuscular and subcutaneous administration is an alternative (col. 9, lines 23-35) From the teaching of Petrus it is evident that glucosamine, its salts and N-acetylglucosamine can be used in a method of treatment of subchondral bone edema via intraarticular or intramuscular administration using a composition in the form of a controlled release too.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a formulation comprising amino sugars in the form of controlled release and use it in a method of treatment of subchondral bone edema as instantly claimed since the active

agents and the methods of treatment via the use of controlled release and modes of administration using them are seen to be suggested in the prior art.

One of ordinary skill in the art would be motivated to administer the active agents in the form of controlled release for the method of treatment as instantly claimed since such a composition overcomes possible adverse gastrointestinal effects seen in oral administration. It will also release the active agent slowly over time. This will prolong the beneficial effect of the active agents.

Response to Applicants Remarks

1. Applicants have traversed the rejection of claims 18-19, 22-24 and 27-28 under 35 USC 102 of record in the previous action arguing that:

Henderson does not teach the positive step of diagnosing a pathological marker associated with a joint condition and does not suggest this step either. The claims are not anticipated by Henderson.

Applicants' arguments are not found to be persuasive. According to Henderson glucosamine administration shows improvement in cartilage integrity in humans with osteoarthritis. Osteoarthritis is a degenerative joint condition marked by cartilage degradation according to Dictionary.com. Henderson's examples show administration of glucosamine compositions to animals having a joint condition. One of ordinary skill in the art knows very well that such a treatment cannot be done unless the biological marker is diagnosed first. Diagnosis is a positive step which is performed to determine the disease or condition which then

followed by the appropriate method of treatment. This is well known in the art and it need not be taught by Hendeson.

2. In response to applicant's arguments the rejection under 35 USC 103 that maintained in the previous office action has been withdrawn and the 103 rejection citing new art is made of record.

Conclusion

Claims 1-30 are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ganapathy Krishnan/

Examiner, Art Unit 1623

/Shaojia Anna Jiang/

Supervisory Patent Examiner, Art Unit 1623